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Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Prior Authorization Review: becaplermin topical gel

Background:
Human platelet-derived growth factor (PDGF) is a substance naturally produced in the body to help in wound healing. It promotes cellular proliferation and angiogenesis, helping to repair and replace dead skin and other tissues by attracting cells that repair wounds.[1] Becaplermin topical gel (Regranex®) is a genetically engineered product that mimics PDGF. It was approved by the U.S. Food and Drug Administration (FDA) in 1997 for the treatment of lower extremity diabetic neuropathic ulcers that have adequate blood supply and extend into the subcutaneous tissue and beyond.[2] The Pharmacy & Therapeutics Committee reviewed this drug previously and approved Prior Authorization (PA) for its use (see **Appendix 1**). The efficacy of becaplermin for lower extremity diabetic neuropathic ulcers has been established in clinical trials and confirmed in post-marketing experience.[3] No other indications have been approved by the FDA.

The efficacy of topical becaplermin has not been established for the treatment of pressure ulcers, venous stasis ulcers, or on exposed joints, tendons, ligaments and bone.[4] Off-label uses include management of necrotic mucosal flap after bone grafting;[5] necrobiosis lipoidica, a necrotizing skin condition is most frequently observed on the shins of both legs of patients with diabetes;[6] and hypertensive leg ulcers;[7] with insufficient or inconclusive evidence.

The FDA issued its strongest warning (Boxed Warning) in 2008 after increased rate of mortality secondary to malignancy distant from the site of application was observed in patients treated with 3 or more tubes of becaplermin gel in clinical studies and post-marketing use.[2] Though this risk has been disputed,[8] the FDA Boxed Warning and associated precautions are still in place.[4]

Recommendations:
No changes to the current PA criteria are recommended. No further review or research needed at this time.

References:
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3. Diabetic Foot Problems, NICE Clinical Guideline 119. National Institute for Health and Clinical Excellence (NICE); March 2011. Available at: http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0041804/pdf/TOC.pdf . Accessed 10 June 2015.
4. Regranex® (becaplermin) [prescribing information]. Fort Worth, TX; Smith & Nephew Inc., August 2014.
5. Calhoun CC, Cardenes O, Ducksworth J and Le AD. Off-label use of becaplermin gel (recombinant platelet-derived growth factor-BB) for treatment of mucosal defects after corticocancellous bone graft: report of 2 cases with review of the literature. *Journal of Oral and Maxillofacial Surgery*. 2009;67:2516-20.
6. Tauveron V, Rosen A, Khashoggi M, et al. Long-term successful healing of ulcerated necrobiosis lipoidica after topical therapy with becaplermin. *Clinical and Experimental Dermatology*. 2013;38:745-47.
7. Senet P, Vicaut E, Beneton N, et al. Topical treatment of hypertensive leg ulcers with platelet-derived growth factor-BB: a randomized controlled trial. *Archives of Dermatology*. 2011;147:926-30.
8. Ziyadeh N, Fife D, Walker AM, et al. A matched cohort study of the risk of cancer in users of becaplermin. *Advances in Skin and Wound Care*. 2011;24:31-39.

Author: A. Gibler, Pharm.D. Date: July 2015

Becaplermin (Regranex®)

Goal(s):

- To restrict use of drugs to conditions funded by the OHP that have demonstrated efficacy.

Length of Authorization:

Up to 6 months

Requires PA:

- Becaplermin topical gel

Approval Criteria		
1. What diagnosis is being treated?	Record ICD9 code.	
2. Is the diagnosis stated as diabetic neuropathic ulcer(s)?	Yes: Go to #3.	No: Pass to RPh. Deny; medical appropriateness.
3. Does the patient take medications for diabetes OR have documentation of diabetes mellitus?	Yes: Approve ONLY 15 grams for 6-month supply.	No: Pass to RPh. Deny; medical appropriateness.

P&T/DUR Review: *7/15; _/_*
Implementation: *_/_*